physical dependence or concurrent tricyclic antidepressant poisoning.

Benzodiazepine cessation may precipitate withdrawal symptoms, depending on the half-life of the specific agent, the duration of use, and the dose. Such withdrawal is characterized by intense anxiety, insomnia, irritability, perceptual changes, hypersensitivity to light and sound, psychosis, hallucinations, palpitations, hyperthermia, tachypnea, diarrhea, muscle spasms, tremors, and seizures. Withdrawal symptoms usually peak 2 to 4 days after the discontinuation of a short-acting agent and 5 to 6 days after discontinuation of a longer-acting one; however, panic attacks and nightmares may recur for months. In general, agents with shorter half-lives produce more intense withdrawal symptoms compared with agents with longer half-lives. Detoxification requires a change to a longer-acting benzodiazepine (e.g., clonazepam, diazepam) or phenobarbital and a tapering regimen of 7 to 10 days for short-acting agents or 10 to 14 days for longer-acting ones. For hemodynamically unstable patients who require very rapid medication titration to control withdrawal symptoms and for those with severe hepatic failure, short-acting medications are indicated in lieu of phenobarbital. Propranolol can be given to decrease tachycardia, hypertension, and anxiety.

*Barbiturates* may be short acting (pentobarbital and secobarbital), intermediate acting (amobarbital, aprobarbital, and butabarbital), or long acting (mephobarbital and phenobarbital). The symptoms of acute intoxication with the withdrawal from barbiturates are similar to those of benzodiazepines. For acute barbiturate overdose, oral charcoal and alkalinization of the urine (to a pH >7.5) with forced diuresis are effective in lowering the blood concentration. For patients with hemodynamic compromise refractory to aggressive supportive therapy, barbiturate elimination can be increased by hemodialysis or charcoal hemoperfusion. The effective treatment of withdrawal symptoms requires estimating the daily dose of the abused drug and substituting an equivalent phenobarbital dose to stabilize the patient, after which the dose of phenobarbital is tapered over 4 to 14 days, depending on the half-life of the abused drug. Benzodiazepines may also be used for detoxification, and propranolol and clonidine may help reduce symptoms.

Abuse of γ-hydroxybutyrate (GHB) has increased substantially over the last decade in the United States. This drug is abused for its sedative, euphoric, and bodybuilding effects. GHB is a metabolite of the neurotransmitter GABA, and it also influences the dopaminergic system. It potentiates the effects of endogenous or exogenous opiates. The ingestion of GHB results in immediate drowsiness and dizziness, with the feeling of a *high.* These effects can be potentiated by the concomitant use of alcohol or benzodiazepines. Similar to flunitrazepam and ketamine, GHB is a popular club drug, and it has been implicated in cases of date rape. Its street names include *G, liquid E, liquid X, fantasy, Georgia home boy, and grievous bodily harm.* Adverse effects that may occur within 15 to 60 minutes of its ingestion include headache, nausea, vomiting, hallucinations, loss of peripheral vision, nystagmus, hypoventilation, cardiac dysrhythmias, seizures, and coma. In rare instances, these adverse effects have led to death. The withdrawal from GHB becomes clinically apparent within 12 hours and may last up to 12 days.

## Opioids

Opioids include the natural and semisynthetic alkaloid derivatives of opium as well as the purely synthetic drugs that mimic heroin. They bind to opioid receptors in the brain, spinal cord, and gastrointestinal tract; in addition, they act on several other CNS neurotransmitter systems, including dopamine, GABA, and glutamate, to produce analgesia, CNS depression, and euphoria. With continued opioid use, tolerance and physical dependence develop. As a result, the user must use larger amounts of the drug to obtain the desired effect, and withdrawal symptoms may occur if use is discontinued. The commonly abused opioids include heroin, morphine, codeine, oxycodone (OxyContin, OxyIR, Oxectya, Roxicodone, or combination products, such as Percocet, Percodan, Tylox, Combunox), meperidine (Demerol), propoxyphene (Darvon), hydrocodone (Vicodin, Lortab, Lorcet), hydromorphone (Dilaudid), buprenorphine (Temgesic) and fentanyl (Sublimaze). In 2000, retail pharmacies dispensed 174 million prescriptions for opioids; by 2009, 257 million prescriptions were dispensed, an increase of 48%. The 2011 National Survey on Drug Use and Health reported that over 70% of subjects who abused prescription pain relievers obtained them from friends or relatives, whereas approximately 5 percent procured them from a drug dealer or over the internet.

Acute opioid overdose produces pulmonary congestion, with resultant cyanosis and respiratory distress, and changes in mental status that may progress to coma. Other manifestations include fever, pinpoint pupils, and seizures. Unsterile intravenous practices can lead to skin abscesses, cellulitis, thrombophlebitis, wound botulism, meningitis, rhabdomyolysis, endocarditis, hepatitis, or human immunodeficiency virus (HIV) infection. Neurologic complications from intravenous heroin use include transverse myelitis, inflammatory polyneuropathy, and peripheral nerve lesions.

For acute opioid overdose, the patient's respiratory status must be assessed and supported. Naloxone should be administered intravenously and repeated at 2- to 3-minute intervals, often in escalating doses; the patient should respond within minutes with increases in pupil size, respiratory rate, and level of alertness. If no response occurs, opioid overdose is excluded, and other causes of somnolence and respiratory depression must be considered. Naloxone should be titrated carefully, since it may precipitate acute withdrawal symptoms in opioid-dependent patients.

Withdrawal symptoms may appear as early as 6 to 10 hours after the last injection of heroin. Initially the individual often has feelings of drug craving, anxiety, restlessness, irritability, rhinorrhea, lacrimation, diaphoresis, and yawning; these signs are followed by dilated pupils, piloerection, anorexia, nausea, vomiting, diarrhea, abdominal cramps, bone pain, myalgia, tremors, muscle spasms, and, in rare cases, seizures. These symptoms and signs peak at 36 to 48 hours and then subside over 5 to 10 days, if untreated. A protracted abstinence syndrome characterized by bradycardia, hypotension, mild anxiety, sleep disturbance, and decreased responsiveness may occur for up to 5 months.

Withdrawal from opioids can be managed with methadone, a long-acting synthetic agonist drug; withdrawal symptoms of methadone develop more slowly and are less severe than those